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Effect of Aqueous Stem Bark Extract of *Parkia Biglobosa* on the Histological Morphology of Liver of Adult Wistar Rats

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ABSTRACT

People in Africa and other developing countries depend on medicinal plants. Extract of *Parkia biglobosa* stem bark is used in Nigerian traditional medicine to treat malaria, diarrhea and pains. This study aimed at determining the effect of aqueous stem bark extract of *P.biglobosa* on the histological morphology of liver in animal models. A total of 28 wistar rats weighing between 100 – 150g were used for this study out of which 12 were used for acute toxicity testing using Lorke's method (1983), the test was carried out in two phases. In phase I, 9 adult wistar rats were divided into 3 groups and administered with 10mg/kg, 100mg/kg and 1000mg/kg orally while in phase II, 3 wistar rats were assigned into 3 groups and administered with 1600mg/kg, 2600mg/kg and 5000mg/kg respectively and both they were observed for signs of toxicity/mortality within 24hrs. The remaining 16 rats were divided into 4 groups; A, B, C and D. Group A served as control and groups B, C and D served as test groups. For 21 days, group A received normal feed and water only and then group B, C and D received oral doses of 1000mg/kg, 500mg/kg and 250mg/kg of aqueous extract of *P.biglobosa* stem bark respectively. A significant increase in the level of ALP, ALT and AST was observed in comparison with the control, P< 0.005 was considered statistically significant. It was shown that liver sections in group A (control) presents no histological changes while the liver section of animals treated with (1000mg/kg and 500mg/kg) of *P.biglobosa* aqueous extract for 21 days revealed an inflammation, vascular degeneration and vacoulation respectively. It was found that at higher doses *P.biglobosa* aqueous stem bark extract could be hepatotoxic.

INTRODUCTION

Parkia biglobosa is a scientific name of African locust bean tree. In Hausa it is referred to as Dorawa, in Yoruba it is known as Igba Irugba and in Igbo it is called Origili. The Parkia tree, named after the famous Scottish botanist and surgeon, Mungo Park by Brown (1826) has long been widely recognized as an important indigenous multipurpose fruit tree in many countries of the sub - saharan Africa.

Parkia biglobosa is found naturally occurring in the following countries of west Africa: Republic of Benin, Burkina Fasso, Cameroon, Chad, Cote d'Voire, Central Africa Republic, Gambia, Ghana, Guinea Bissau, Kenya, Mali, Niger, Nigeria, Senegal, Sierra Leones, Sudan, Togo, Tanzania, Uganda and Zaire (Booth and Wickens, 1988) (Sina & Traore, 2002).

In Nigeria, *Parkia biglobosa* is found in the Savannah zone with the bulk of it in the Guinea Savannah. This is as a result of its ecological and environmental requirements which are easily met in these areas (Oni, 1997).

The distribution of *Parkia biglobosa* in Nigeria covers Abuja, Adamawa, Bauchi, Gombe, Kaduna, Kano, Katsina, Kebbi, Kogi, Kwara, Nassarawa, Niger, Oyo, Taraba, Yobe, Plateau and Zamfara state.

In west Africa the bark, roots, leaves, flowers, fruits and the seeds are commonly used in traditional medicine to treat a wide diversity of complaints, internally and externally, sometimes in combination with other medicinal plants (Builders *et al.*, 2011). The bark is the most important for medicinal uses, followed by the leaves. It have been used in Nigeria and other west African rural communities to treat a variety of diseases (Abbie 1990; Shao 2002).

The bark soaked in ethanol are also used in some communities for anti diarrhoeal properties and as an effective anti-snake venoms that protects against neurotoxic, haemotoxic and cytotoxic effects of poisonous snake (Agunu *et al.*, 2005).

The efficacy of the various preparation of *Parkia biglobosa* is widely acclaimed by Hausa communities of northern Nigeria for the treatment of diseases such as Malaria, diabetes mellitus and pains.

The bark is boiled in water and taken as a decoction for the treatment of malaria, inflammatory disease and infection to diarrhoea (Asase *et al.*, 2005; Gronhaug *et al.*, 2008; and Tijjani *et al.*, 2009).

A decoction of the stem - bark is used as a mouth wash to relieve tooth ache as well as, a bath for fever (Ajaiyeoba 2002). The bark is also used with lemon for wounds and ulcers. In Cote d'voire, a bark infusion is used as a tonic for diarrhoea and as an enema (Duker - Eshun *et al.*, 2018; Agunu *et al.*, 2005).

Among the Hausa people of northern Nigeria, *Parkia biglobosa* is used against bronchitis, Pneumonia, diarrhea, vomiting, sores and Ulcers.

The water extract demonstrated increase in the triglyceride and cholesterol level. Phytochemicals

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generally are regarded as research compounds. Some phytochemicals have been used as poisons and others as traditional medicine (James *et al*., 2007). Parkia plants have been identified as source of tannins, saponins, steroids, Reducing sugars and Glycosides.

There is increased research in to phytochemical for the effective therapeutic combat of this menace. The therapeutic effects of plant - based drugs have been documented to be due to the phytochemicals that constitute the plants (Kumar *et al*., 2012).

MATERIALS AND METHOD

Research Design

The study was randomized control trial (an experimental study) and the ethical approval for the research was obtained from the Research ethical committee, College of Health sciences, Bayero university Kano, Kano state.

Preparation of Experimental Animals

Twenty-eight (28) healthy Adult wistar rats of both sexes weighing (100 - 150g) were purchased from the Animal House section of the Department of Pharmacology, Faculty of Pharmaceutical Sciences, Bayero University, Kano. The animals were maintained in standard animal cage at the Pharmacology Department and also they were acclimatized for 2 weeks prior to the commencement of the study. The animals were allowed to have free access to drinking water and standard livestock feed, also the animals were maintained under standard condition of humidity and temperature.

A standard protocol were adhered in accordance with the Good Laboratory Practice (GLP). The principle of Laboratory animals care were also be followed in this study.

Preparation of Aqueous Extraction of *Parkia Biglobosa*

The stem bark of *Parkia biglobosa* were collected from Gabasawa local Government area of Kano State. A quantity of stem bark was allowed to air dried under shade at room temperature. Using wooden mortar and pestle, the dried stem bark was grinded to powder form. Five hundred (500) grams of the powdered material were soaked in three liters (3L) of distilled water and were allowed to stand for 120 hours (5 day).

The mixture were filtered using a Whatmann's filter paper to obtained the extract. The filterate were then incubated in water bath and evaporated under reduced pressure, the filterate was allowed to dried in a hot air oven at 40oc to give 75g of an aqueous stem bark extract which were used for interventional study at different doses.

Qualitative Determination of Phytochemical Substances of *Parkia Biglobosa* Aqueous Stem Bark Extract

A small portion of the extract was subjected to phytochemical test. Methodologies for the determination of Phytochemical substances used in this research were adapted from those reported by Keay *et al.* (2008) and Ejikeme *et al.* (2014)

Acute Toxicity Testing

The LD50 of the extract was determined using Lorke's method (1983). The test were carried out in two phases;

In phase I, nine (9) wistar rats was randomly assigned into three (3) groups of three (3) wistar rats each. The first (1st) group comprised of wistar rats weighing 126g, 140g and 135g respectively and they were administered with 10mg/kg body weight of the extract using orogastric tube (oral cannula).

The 2nd group comprised of wistar rats weighing 152g, 143g and 136g respectively and they were given 100mg/kg and the 3rd group comprised of wistar rats weighed 122g,131g and 138g respectively and they were given 1000mg/kg body weight of the extract. The animals was observed within 24 hours to monitor the behavioral changes for signs of toxicity as well as mortality.

In phase II, three (3) rats weighing 148g, 151 and 153g respectively was used and randomly placed in to 3 groups of one (1) wistar rat each. The animals were administered with high doses of 1600mg/kg, 2900mg/kg and 5000mg/kg respectively. They were then observed within 24 hours for signs of toxicity and mortality. After 24 hours, there was no any mortality in both Phase I and II of the experiment.

Therefore, 20% of the highest dose (5000mg/kg) used for the LD50 was used as the highest dose (1000mg/kg) in this experiment. 10% of 5000mg/kg was used as the medium dose (500mg/kg) and 5% of 5000mg/kg was used as low dose (250mg/kg) in the experiment.

Animal Grouping and Intervention

Sixteen (16) rats were randomly selected and then divided in to Four (4) groups, labeled as group A, B,C and D; with each group containing Four (4) wistar rats. The groups constitute of three (3) test groups and control group. The animals in group A were used as the control group and therefore they were not received any intervention rather they were administered with distilled water in place of the intervention. The animals in group B were used as the first test group and were administered with high dose (1000mg/kg) of the aqeous stem bark extract of *Parkia biglobosa* orally every day for a period of three (3) weeks.

The animals in group C were administered with medium dose (500mg/kg) of the *Parkia biglobosa* aqueous stem bark extract for a period of three weeks. The animals in group D were used as another test group and they were administered with low dose (250mg/kg) of the *Parkia biglobosa* aqueous stem bark extract orally for a period of three weeks.

All the four (4) groups were maintained for a period of three weeks.

Therefore, measurement of the animals weight was done before the commencement of the experiment, weekly and after administration of the *Parkia biglobosa* aqueous stem bark extract.

Liver Function Test (LFT)

After 3 weeks of the experiment, a blood sample were

obtained from orbital venous plexus, and the blood samples were collected in to a plain tubes, they were allowed to clot and centrifuged at 1500 rpm for 15 minutes. The serum were obtained after separation and then used for determination of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and Alkaline phosphatase (ALP).

Preparation And Processing of the Organ (Liver)

On the Final day of the intervention, the animals was sacrificed by cervical dislocation. The liver was harvested and then fixed in 10% formalin for 48 hours and label with tags. Gross anatomy of the liver was studied first to identify any observational lesion before subjecting the tissue into the tissue processing protocol. The processed tissues were embedded in paraffin wax and tissues section of three (3) microns were cut using Leica brand microtome .

The histological sections floated out in tissue water bath, picked with a glass slide and stained with Hematoxylin and Eosin staining technique for demonstration of the tissue architecture and examination.

Data Analysis

Result was presented in a tabular form and photomicrographs were attached to the result obtained. All test group of the animals was compared with the control group using one-way ANOVA, using the computer programme Statistical Package for Social Sciences (SPSS) software version 20, Post hoc comparison were the method used for the analysis. All data were expressed as mean ± standard error of mean (SEM) and $P<0.005$ was considered statistically significant.

RESULTS

Physical Property of Stem Bark Extract of *Parkia biglobosa*

The aqueous extract was obtained by dissolving 500g of the *Parkia biglobosa* stem bark powder in to 3Liters of distilled water. The extraction procedure yielded 75g of the extract and the percentage yield was calculated as 15% while physical properties of the extracts are cocoa-brownish in colour, crystalline shiny in consistency with a sweet smell.

Table 1: Physical properties of *Parkia biglobosa* stem bark extract

Plant part	Extract type	% Yield	Texture	Colour	Smell
Stem bark	Aqueous extract	15%	Crystalline	Cocoa-	Sweet
			Shiny	Brownish	Smell

Phytochemical Analysis

The Phytochemical screening of Parkia boglobosa aqueous stem bark extract were carried out to determine the presence of the following Compounds: Tannin, Saponin, Reducing sugars, Steroids and Phenols using a standard procedure reported by Keay *et al*., (2008) and Ejikeme *et al*., (2014).

Table 2: Phytochemical screening of the Aqueous stem bark extract of *Parkia biglobosa*

Phyto-constituents	Test method	Result
Tannin	Aqueous extract	+
Saponin	Ferric chloride test	+
Flavonoid	Ammonium hydroxide method	-
Cardiac glycoside	Keller Killiani's test	-
Reducing sugars	Ferric chloride test	+
Steroids	Salkowski's test	+
Terpenoids	Salkowski's test	-
Phenol	Ferric chloride test	+

Note: '+' represents Phytoconstituent present, '-' represents Phytoconstituent absent.

Acute Toxicity Evaluation

The aqueous extract administered to the wistar rats showed no sign of toxicity or behavioral changes. After 24 hours observation, no death were recorded in both phase I and phase II of the experiment. Therefore, the Lethal Dose (LD50) of the aqueous stem bark extract of *Parkia biglobosa* was greater than 5000mg/kg body weight as described in Table 3.

Table 3: Lethal Dose (LD50) of Aqueous stem bark extract of *Parkia biglobosa* in wistar rats

Dose (mg/kg)	Sign of Toxicity/Mortality Result	
	Phase I	Phase II
10	0/3	-
100	0/3	-
1000	0/3	-
1600	-	0/1
2900	-	0/1
5000	-	0/1

The LD50 of the Aqueous stem bark extract was determined using Lorke's method (1983)

Effect of Aqueous Stem Bark Extract of *Parkia Biglobosa* on Weight of the Experimental Animals Before (Pre) and After (Post) Interventional Study According to the Doses Administered

During the interventional study, the weight of the animals was recorded before and after the study. The mean of the weights of the animals before intervention of all the groups were found to be 105.50 for group A (control),

135.25 for group B, 122.50 for group C and 131.00 for group D.

These result clearly indicates that there are increase in mean of the weights from group A to B before intervention. The mean of the weights of the animals after intervention of group A to D were found to be 119.25 for group A (control), 163.00 for group B, 129.00 for group C and 174.00 for group D.

The body mean weight difference between the groups are; 13.75 for group A, 27.75 for group B, 6.50 for group C and 43.00 for group D. These result clearly indicates that there is slightly increase in body weight across all groups.

Table 4: Effect of aqueous stem bark extract of *Parkia biglobosa* on weight (Mean ± SEM) of the wistar rats before (pre) and after (post) interventional study according to the doses administered

	Pre- Weight	**Post-Weight**
Group A	105.5 ± 3.57	119.25 ± 7.79
Group A	135.25 ± 15.48	163.0 ± 21.79
Group A	122.5 ± 12.20	129.0 ± 5.85
Group A	131.0 ± 8.91	174.0 ± 10.00

Group A = Control Group, Groupn B = High dose of aqueous stem bark extract of Parkia biglobosa (1000 mg/kg), Group C = Medium dose of aqueous stem bark extract of Parkia biglobosa (500 mg/kg) and Group D = Low dose of aqueous stem bark extract of Parkia biglobosa (250 mg/kg).

Liver Function Test (Liver Enzymes)

Table 5: Comparison of liver enzymes (Mean ± SEM) among different test groups and control group

Parameter	**Group A**	**Group B**	**Group C**	**Group C**	**Group D**
ALP (IU/L)	48.00 ± 3.24	90.00 ± 2.08	67.00 ± 3.05	53.50 ± 4.50	0.000
ALT (IU/L)	23.25 ± 1.65	46.66 ± 2.33	41.00 ± 1.15	27.50 ± 1.50	0.000
AST (IU/L)	23.75 ± 2.95	45.66 ± 2.02	38.33 ± 4.33	30.00 ± 3.00	0.001

The result were expressed as Mean ± SEM and $P < 0.005$ is statistically significant

Histological finding on liver of group A (control) and test groups (Group B, C and D)

The liver sections of control group (Group A) shows no observable changes with hepatocytes radiating from a distinct central vein. None of the tissue sections from this group showed any histomorphological changes (Figure A). Group B shows area of inflammation and vascular degeneration (Figure B). Group C shows an areas of inflammation, degeneration and vacuolation of hepatocytes (Figure C). Group D shows no observable changes indicating that there is no evidence of liver cell damage (Figure D).

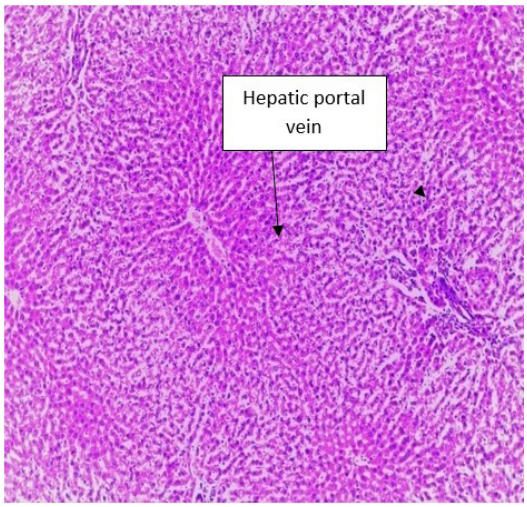

Figure 1: A Photomicrograph of liver section from group A (control) which shows normal hepatic portal vein

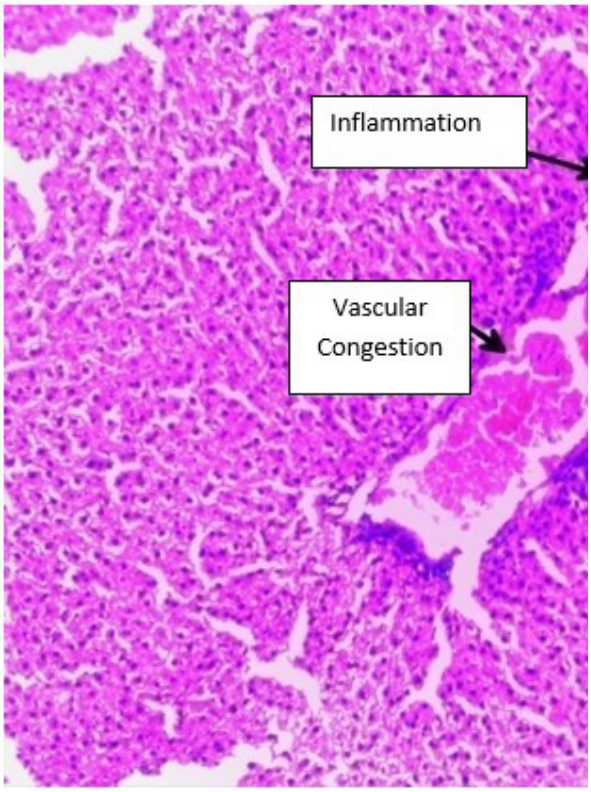

Figure 2: A Photomicrograph of liver section from group B (1000mg/kg) showing areas of inflammation and vascular congestion obtained using H&E Staining technique (mag×100)vein

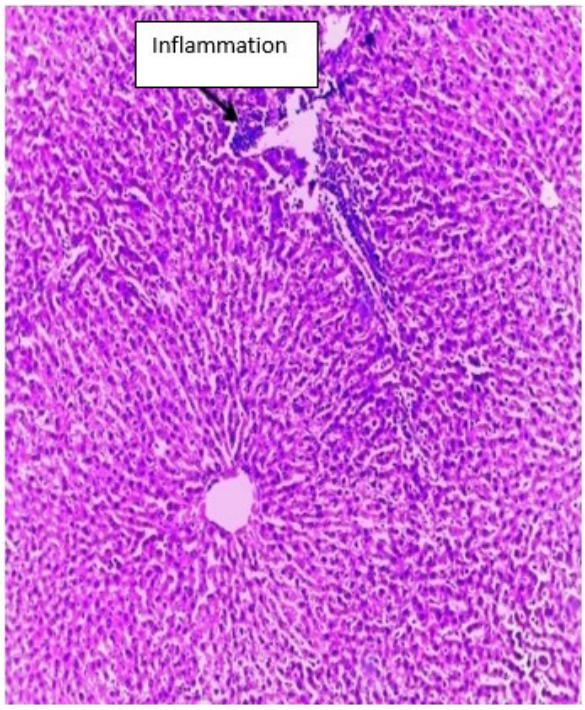

Figure 3: A Photomicrograph of liver section from group C (500mg/kg) which shows areas of inflammation and Hepatic portal vein obtained using H&E Staining technique (mag×100) vein

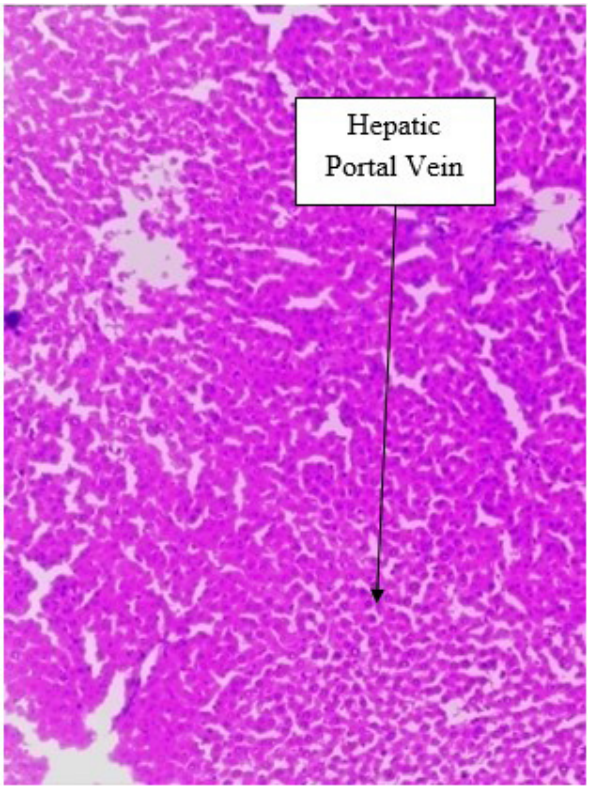

Figure 4: A Photomicrograph of liver section from group C (500mg/kg) which shows areas of inflammation and Hepatic portal vein obtained using H&E Staining technique (mag×100) vein normal hepatic portal vein obtained using H&E Staining technique(mag×100)

Figure 5: Photomicrograph of stem bark of *Parkia biglobosa*

DISCUSSION

In this study, the extraction procedure yielded 75g of the dried extract and the percentage yield were calculated as 15% which were used for interventional study at various doses.

The acute toxicity of *P. biglobosa* has been investigated to determine any adverse effect that may arise as a result

of a short time animal exposure to the extracts within 24 hours period. Though *P.biglobosa* has been used by Traditional medical practitioners (TMPs) without report of any mortality due to toxicity, this claim has been authenticated by the lack of death at oral treatment of over 5000 mg/kg body weight of the extract. The results thus suggest that the extract of *P. biglobosa* has low toxicity (Schorderet, 1992), since the LD50 was greater than 5000mg/kg body weight. The low toxicity obtained may have been responsible for its widespread use in different ethnotherapeutic interventions.

Rats treated with various doses of the extract (1000 mg/kg, 500 mg/kg and 250mg/kg) showed a significant increase in body weights in relation to the control animals, indicating that *P. biglobosa* has adverse effects on the body weight. The water extract increases serum triglycerides concentration and total cholesterol level.

Ordinarily, liver cell damage is characterized by a rise in plasma enzymes (ALP, AST, ALT, etc). In this study, there is a slightly increase in liver enzymes level (AST, ALT and ALP) compared to the control group. The group treated with high and medium doses shows a slight increase in the level of the enzymes and also the histological investigation reveals an inflammation and vascular degeneration, therefore *P. biglobosa* induces hepatocellular damage.

The plant kingdom represents an enormous reservoir of biologically active compounds with various chemical structures and protective /disease preventive properties (phytochemicals). These phytochemicals, often secondary metabolites present in smaller quantities in higher plants, include the alkaloids, steroids, flavonoids, terpenoids, tannins, and many others. The active principles of many drugs found in plants are secondary metabolites (Ghani, 1990; Dobelis, 1993). Therefore, basic phytochemical investigation of these extracts for their major phytoconstituents is also vital. In this study, the aqueous stem bark extract of *P.biglobosa* revealed the presence of tannin, Saponin, reducing sugars, phenol and steroids.

The toxic effect of water extract of *P. biglobosa* on the liver may be due to any one or more of the phytochemicals present in the extract. Furthermore the phytochemical screening of the water extract of *P. biglobosa* indicated presence of appreciable amount of tannins. Study conducted by Yamasaki *et al.* (2002), Bajaj (1988), showed that a large intake of tannins may cause liver damage.

In this study, it was found that in control group no morphological changes were identified by histopathology in the liver suggesting that these animals were healthy and the condition under which the experiment was conducted were proper.

The animals administered with high dose of *P.biglobosa* stem bark extract (1000mg/kg) showed areas of vascular degeneration as shown in the photomicrograph in figure B. The animals treated with medium dose of *P.biglobosa* stem bark extract (500mg/kg) showed a considerable sign of inflammation, degeneration and vacuolation of hepatocyte. as shown in the photomicrograph in figure C.

The animals administered with low dose of water extract of *P.biglobosa* (250mg/kg) showed no remarkable liver cell damaged and no any sign of inflammation as shown in figure D.

CONCLUSION

This study has shown the diversity in toxicity as well as the chemical constituent of the aqueous stem bark extract of *P. biglobosa*. There is slight increase in serum liver enzymes (ALP, ALT and AST) and the histological investigation revealed some areas of inflammation and vascular degeneration which shows an evidence of liver injury due to the consumption of *P.biglobosa*. However this study provides the basis for further studies on the detailed toxic and pharmacological effects of the extracts of *P. biglobosa* stem bark and their active compounds.

RECOMMENDATION

1. There is a need for making a societal awareness on the pathological condition of liver that could arise with unspecific consumption of aqueous stem bark extract of *Parkia biglobosa*
2. Further research could be taken and executed using different extraction solvent such as Methanol or Ethanol to note if there will be a significant changes in the diversity of toxicity as well as the chemical constituent(s) of the stem bark extract of *Parkia biglobosa*
3. A lot of information on the adverse effects of the extract has to be establish.

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